A Functional Role for the Minicolumn in Cortical Population Coding

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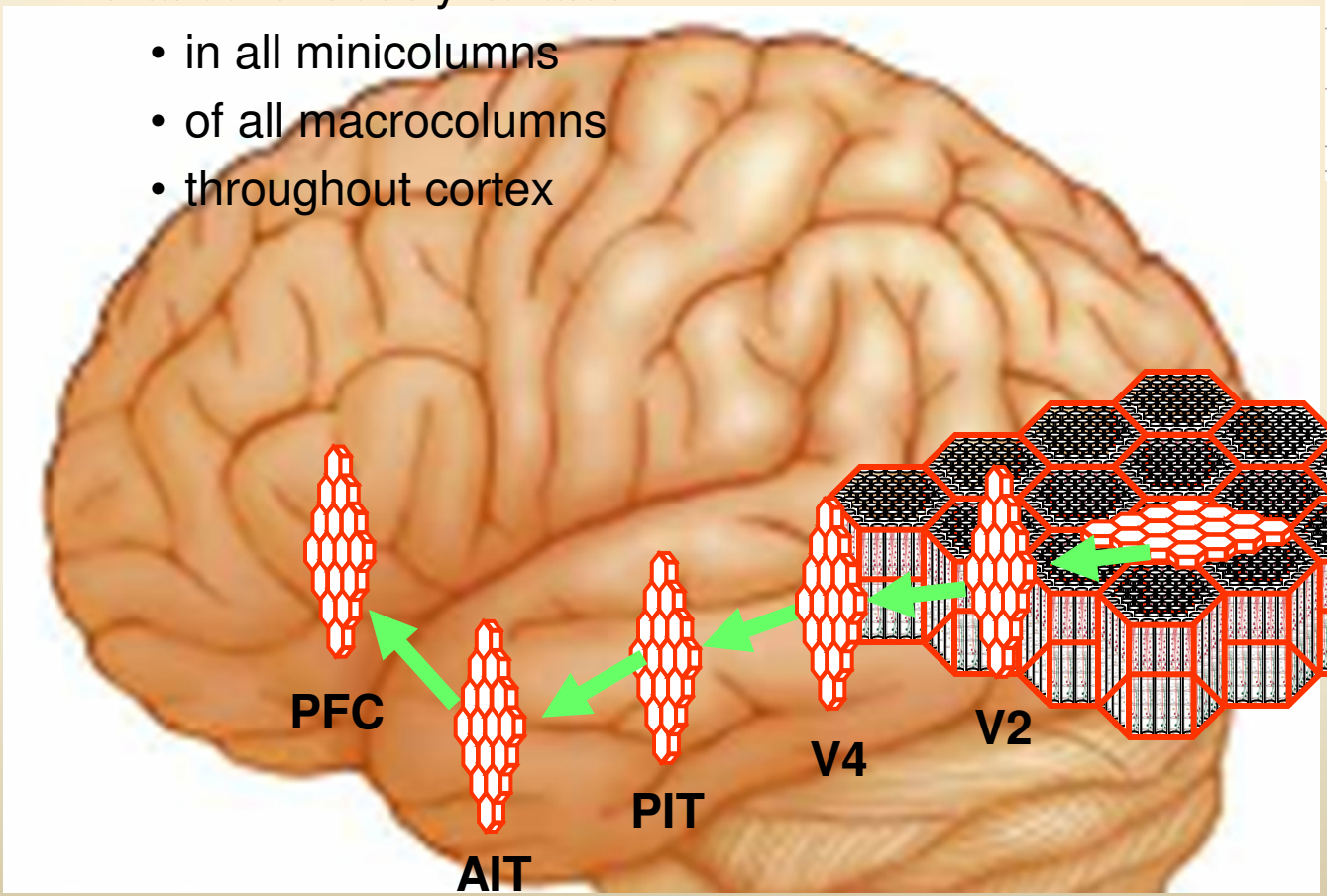
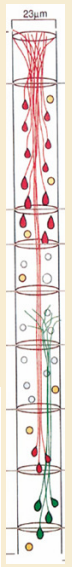
Generic Information Processing Algorithm

…that continuously iterates:

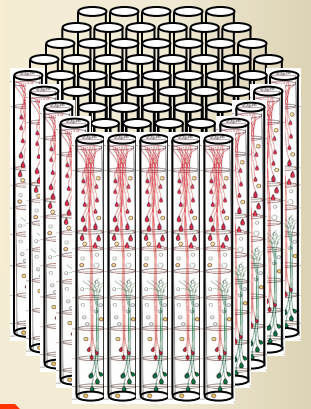
- in all minicolumns
- of all macrocolumns
- throughout cortex





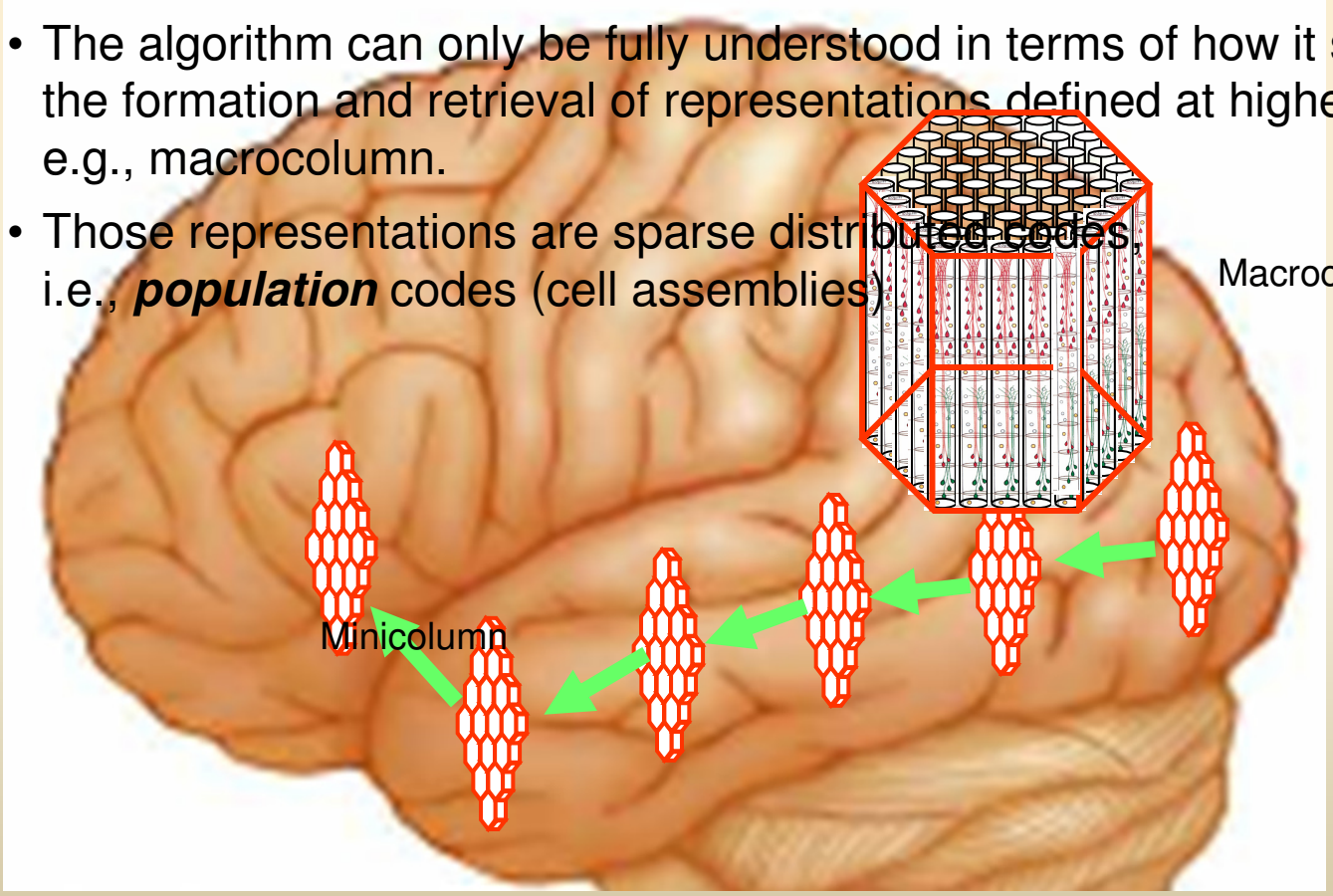
Minicolumn
~100 cells

Macrocolumn
~70 minicolumns



“Canonical Cortical Microcircuit”

- The algorithm includes processes local to the minicolumn.
- But, involves global mechanisms as well
  - Neuromodulators: NE, Ach, DA
- The algorithm can only be fully understood in terms of how it supports the formation and retrieval of representations defined at higher scales, e.g., macrocolumn.
- Those representations are sparse distributed codes, i.e., ***population*** codes (cell assemblies)



Canonical Microcircuit Algorithm: Overview

1. Winner-take-all (WTA) competition in the minicolumn
   - No direct evidence for this…resolution not available yet
2. Global measure of familiarity, *G*, over multiple minicolumns, e.g., over the macrocolumn
3. Increased expansivity of principal neurons' sigmoidal activation function in direct proportion to *G*. This increases chances of reactivating the closest matching previously stored code in the macrocolumn
4. Occurs in a gamma cycle (~20-30 ms)
   - cf. Fries et al. (2007) …WTA in a gamma cycle…

Largely Uncharted Territory

1. There are relatively few functional models of the minicolumn.
    - Some concern processing of specific information
        - Favorov & Kelly (1994a,b)
        - Edgar Körner's group (HRI)
        - Lücke & Malsburg (2004)
        - Rinkus (1996 to pres.)
        - Fransén & Lasner (1998)
    - Some concern more general operational properties
        - imbalance of excitation and inhibition in autism/schizophrenia (Casanova and colleagues)
2. The macrocolumn has been both anatomically and physiologically (functionally) characterized, e.g., in terms of receptive field tuning.
3. The minicolumn has mostly been characterized anatomically.
    - However, see Favorov and colleagues' work
4. "a structure without a function"
    - Horton & Adams (2005)

Largely Uncharted Territory

Anatomical data on columns

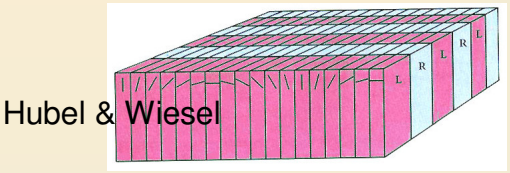
- Macrocolumns
- Minicolumns

Cortical microcircuit data

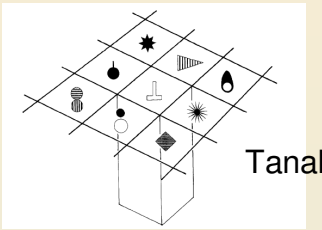
- Huge body of data on connectivity and physiology of cortical principal cells and interneurons.

Physiological data on columns

- Hypercolumns
- Segregates



Hubel & Wiesel



Tanaka

Functional model of the minicolumn
i.e., how the minicolumn functions in the storage and retrieval of *specific* patterns.

Hippocampal data

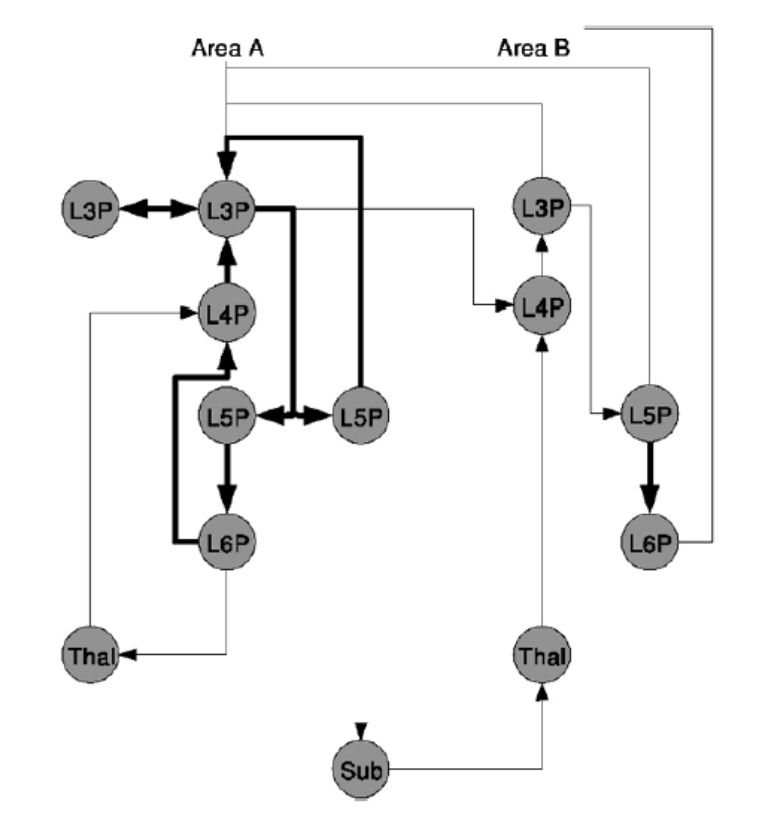
- if the hippocampus is functional analog of small patch of cortex
  - E.g., Tukker et al. (2007)

Cortical rhythms

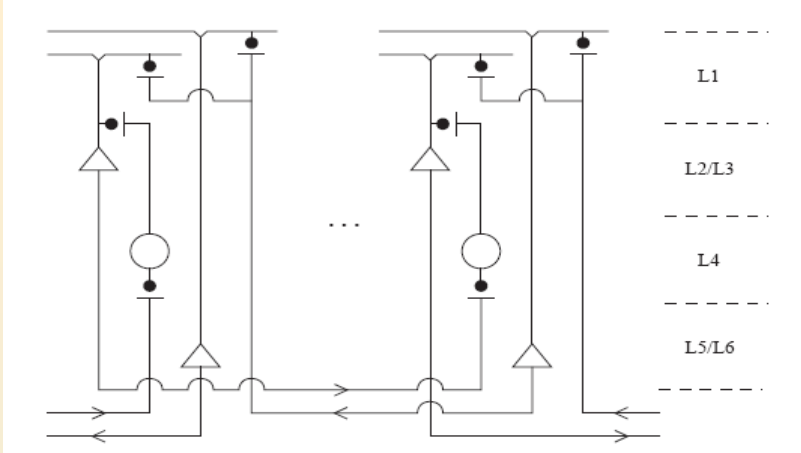
- Gamma cycle as WTA operation

Cortical Microcircuit Models

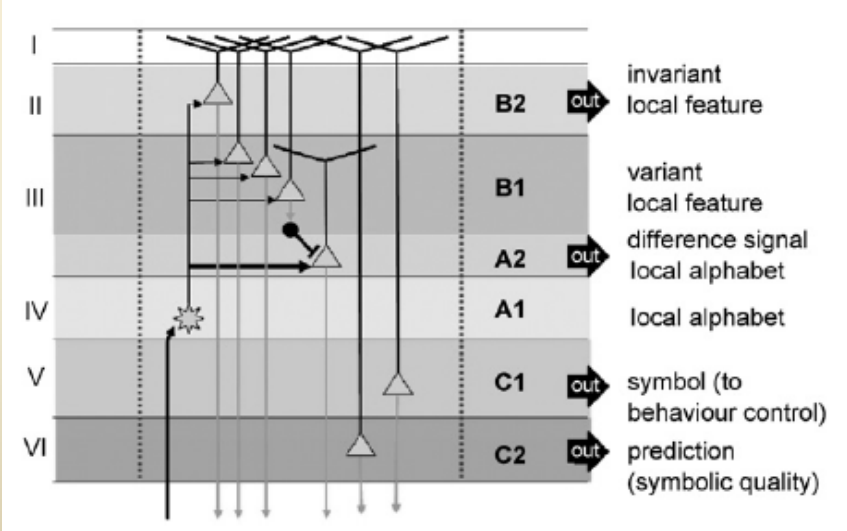
- FF (e.g., thalamus) → L4 → L2/L3 → L5/L6
- Higher-order regions (top-down) feedback: L5 to L1
- Usually no specific mention of minicolumn
- Almost always framed using a localist representation of cell types



- Binzegger, Douglas & Martin (2004)



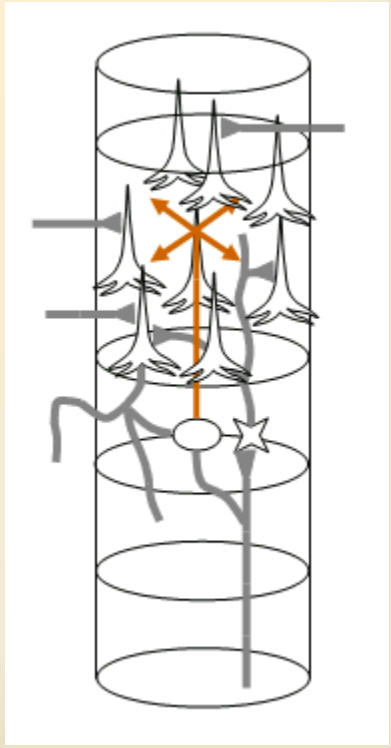
- Dean (2005)



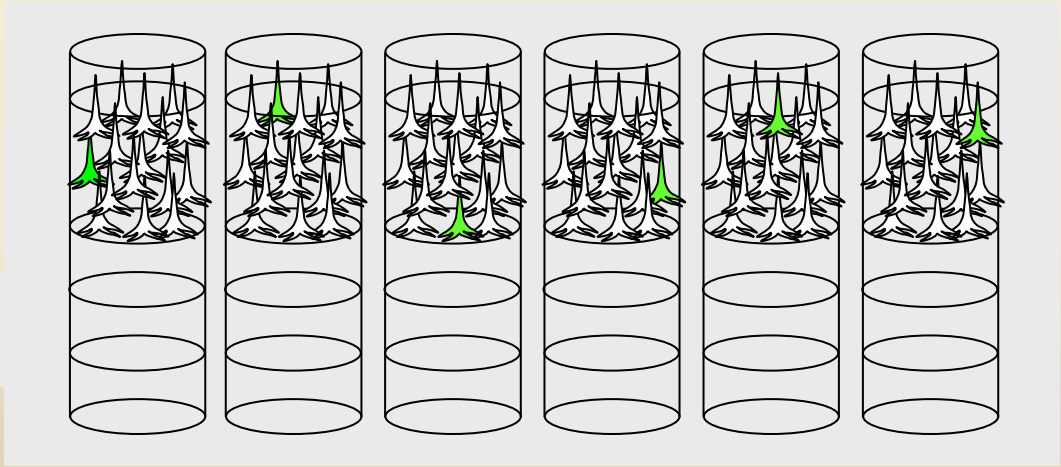
- Knoblauch et al. (2007)

Proposed Minicolumn Function: Local Perspective

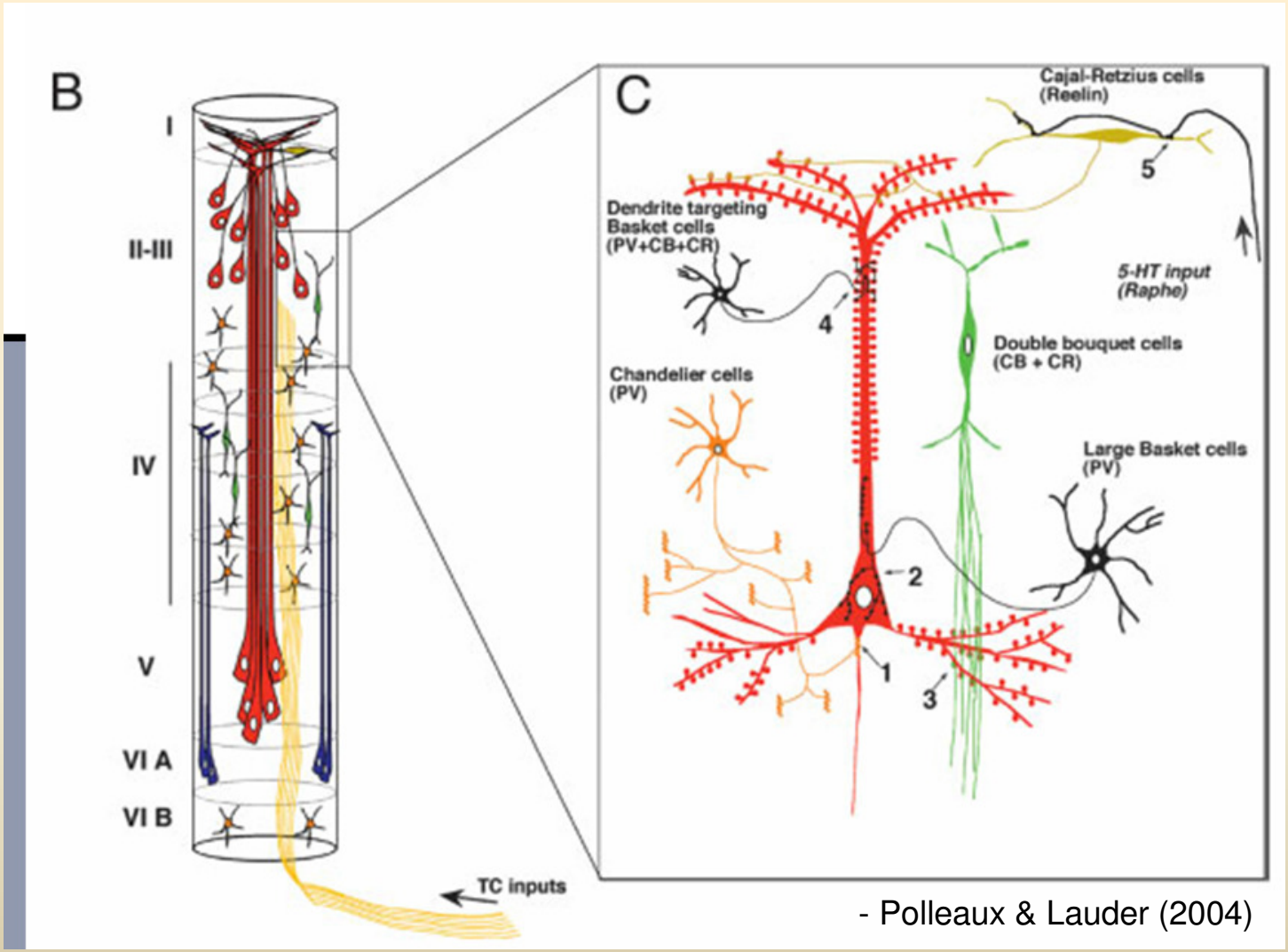
- Minicolumn functions as a winner-take-all (WTA) Module
  - One principal cell becomes active (wins) in each discrete processing cycle.
  - Processing cycle ≈ 30 ms…..gamma cycle.
- Processing occurs simultaneously, and in phase, in all of the macrocolumn's minicolumns.
- In each cycle, the ***set*** of winners in the macrocolumn constitutes a sparse ***population code*** within that macrocolumn.



Small macrocolumn
(6 minicolumns)



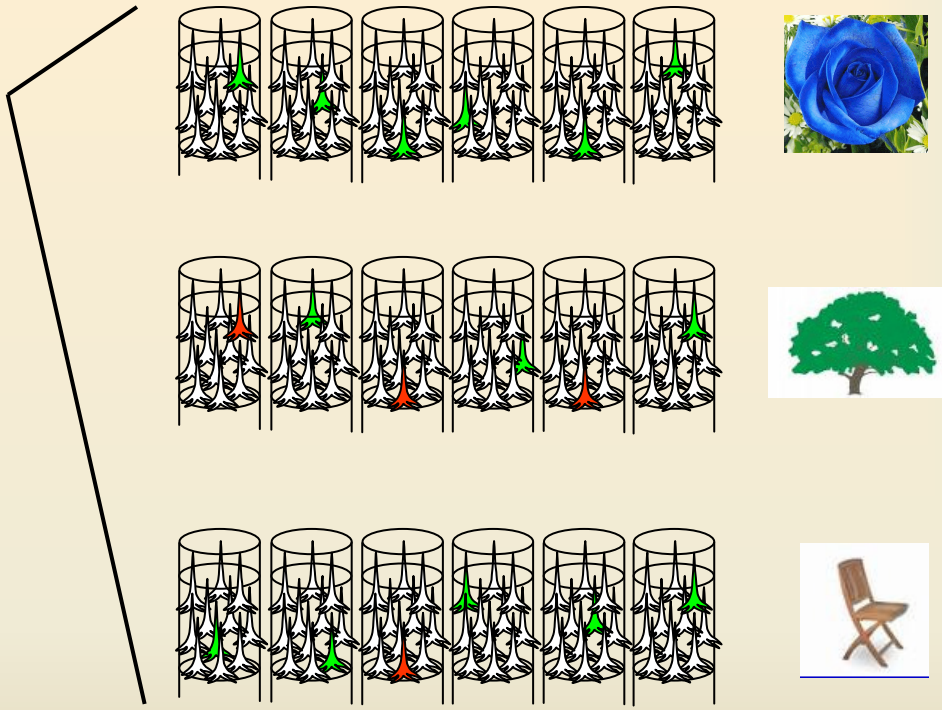
Very Coarsely Mapped to Anatomy



- Polleaux & Lauder (2004)

Advantages of Sparse Population Codes?

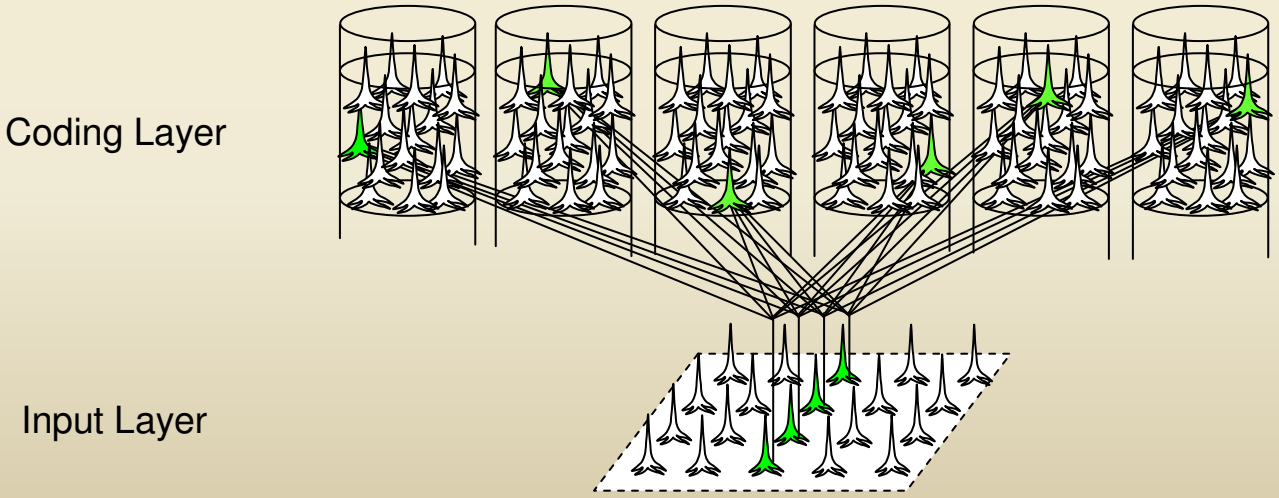
1. Similarity of input patterns can be represented by degree of overlap between representations
2. Which in turn allows single-step retrieval of the best-matching stored representation, i.e., the maximum likelihood hypothesis.
3. Higher capacity
4. Robustness to cell death



# of unique codes = 10^6 vs. 60

Proposed Minicolumn Function: Global Perspective

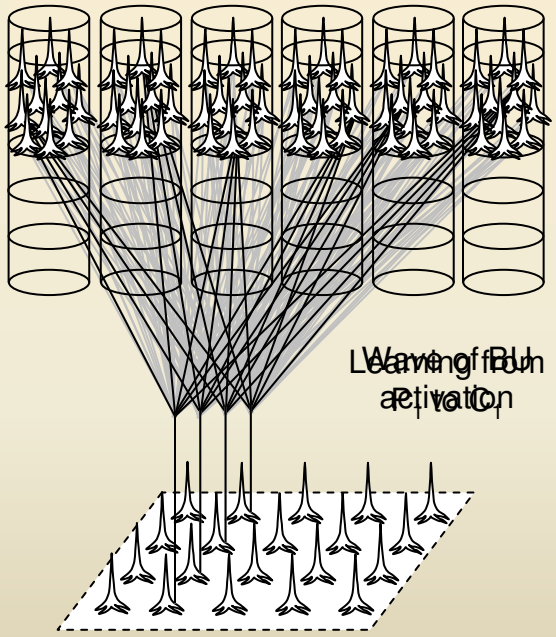
- Individual minicolumns function as WTA modules.
- ***But***, how do ***multiple*** minicolumns function as a unit?
- What could ***bind*** together the simultaneous winners across multiple minicolumns into a permanent population code?
- ***Answer:***
  - Coactivity and the coordinated learning that occurs during the coactivity.
  - A ***global*** (e.g., macrocolumn-level) measure of the familiarity of the current input.
  - A process by which that measure influences which cells win in each minicolumn.



The Need for a Familiarity Measure

Learning

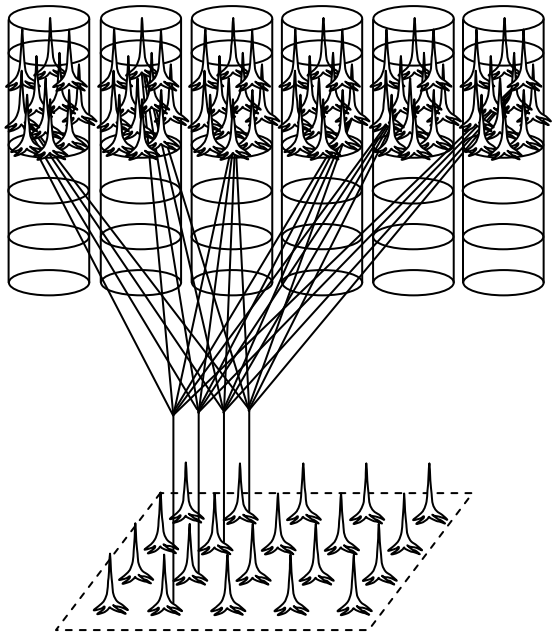
Six winners, code C_1, are chosen randomly



Input pattern, P_1, is presented

Test: Familiar

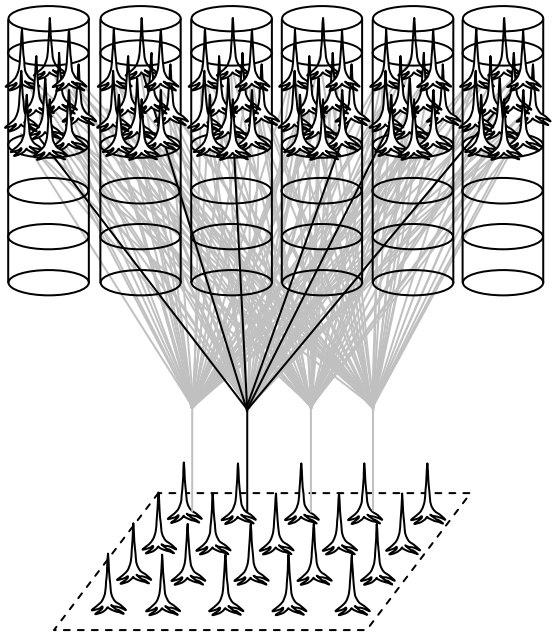
- C_1 cells have high bottom-up (BU) summations
- Desired behavior is that all C_1 cells should be reactivated



P_1 presented again

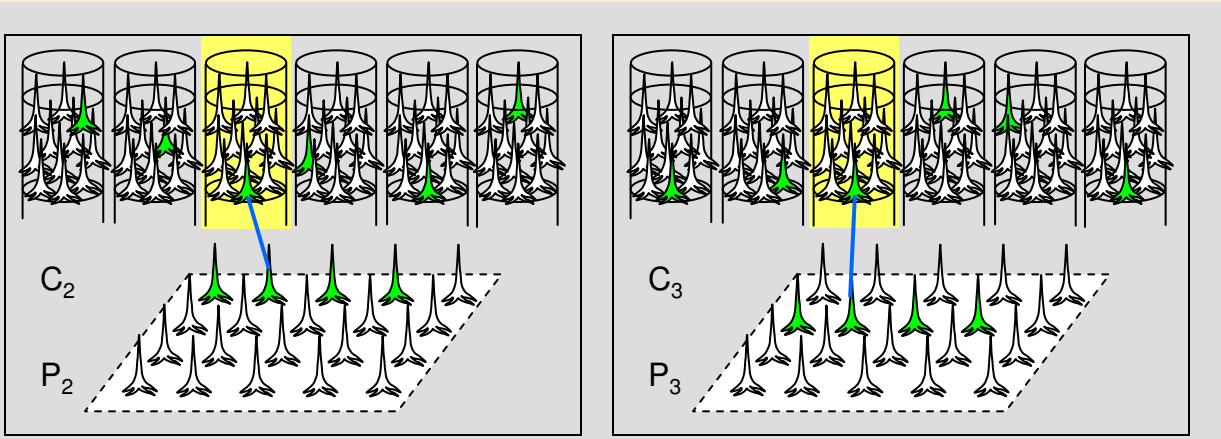
Test: Novel

- C_1 cells have low, but still maximal, BU summations
- Local WTA would reactivate the entire C_1 code
- Desired behavior is that C_2 has small overlap with C_1

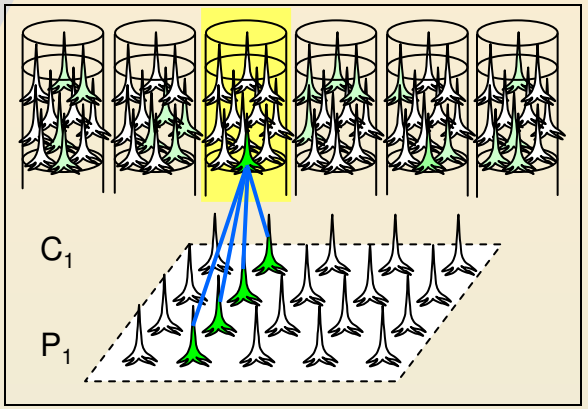


Novel input, P_2, presented

Why average over all minicolumns in a macrocolumn?



First, learn these four associations



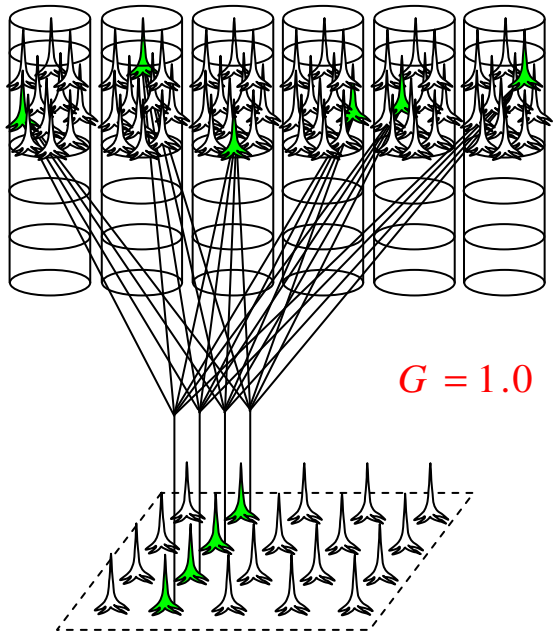
Then, test this novel input

- From the highlighted mincolumn's point of view P_1 is completely familiar.
- But clearly, it should be deemed extremely novel.
- Making the choice of winner in any single minicolumn depend on average conditions across multiple minicolumns, allows overall distributed code to act coherently.

How can global familiarity, G, be computed?

- Compute average of the cells with the max normalized summations in their respective minicolumns

C_1 cells have ***high*** BU summations



Test: Familiar

Potential (1)

$$v(i) = \sum_{k \in P} a(k) \times w(k,i)$$

Normalized Potential (2)

$$V(i) = v(i) / Z_1$$

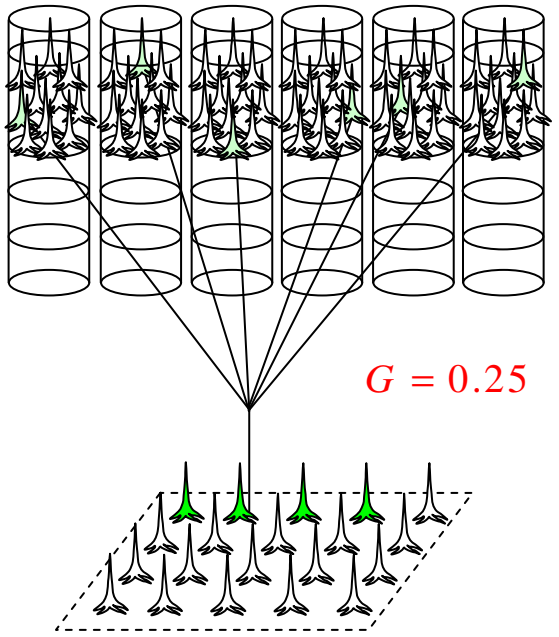
Max Normalized Potential in j^{th} minicolumn (3)

$$\hat{V}_j = \max_{i \in M_j} \left(V(i) \right)$$

Average Max Normalized Potential over all minicolumns (4)

$$G = \sum_{j=1}^{j=6} \hat{V}_j \Big/ Z_2$$

C_1 cells have ***low*** BU summations



Test: Novel

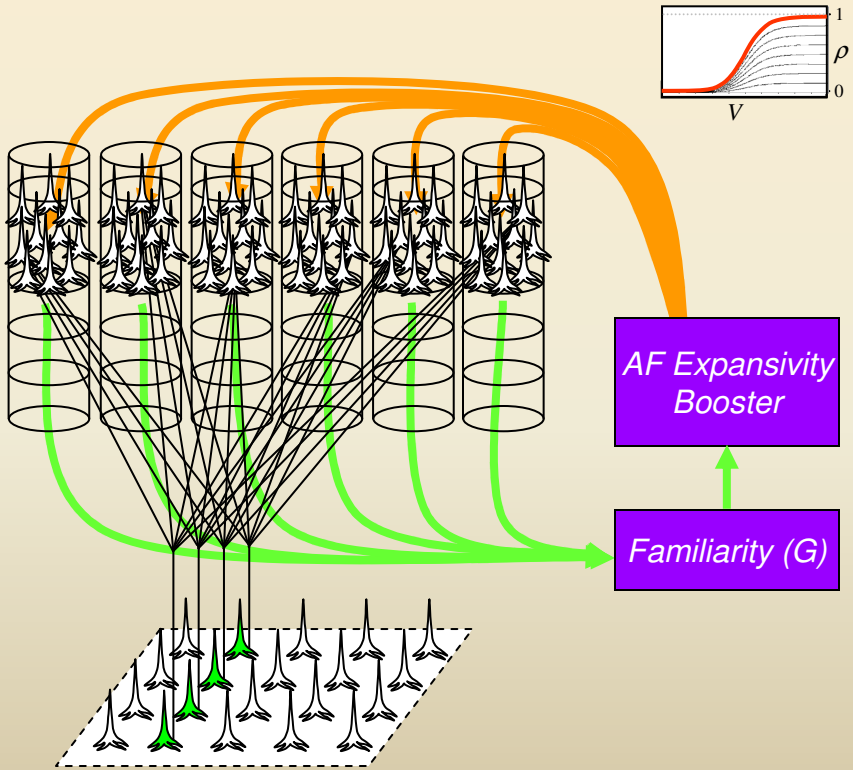
- **Z_1 = # of active cells in an input pattern (cf. "Adaptive Regulation of Sparseness by Feedforward Inhibition" - Assisi et al, 2007)**
- **Z_2 = # of minicolumns**

What to do with G?

Highly familiar input (G ≈ 1)

Should reactivate the code of the closest matching previously stored input. Indeed, it is the synaptic increases onto the cells comprising that code, which has caused the high G value.

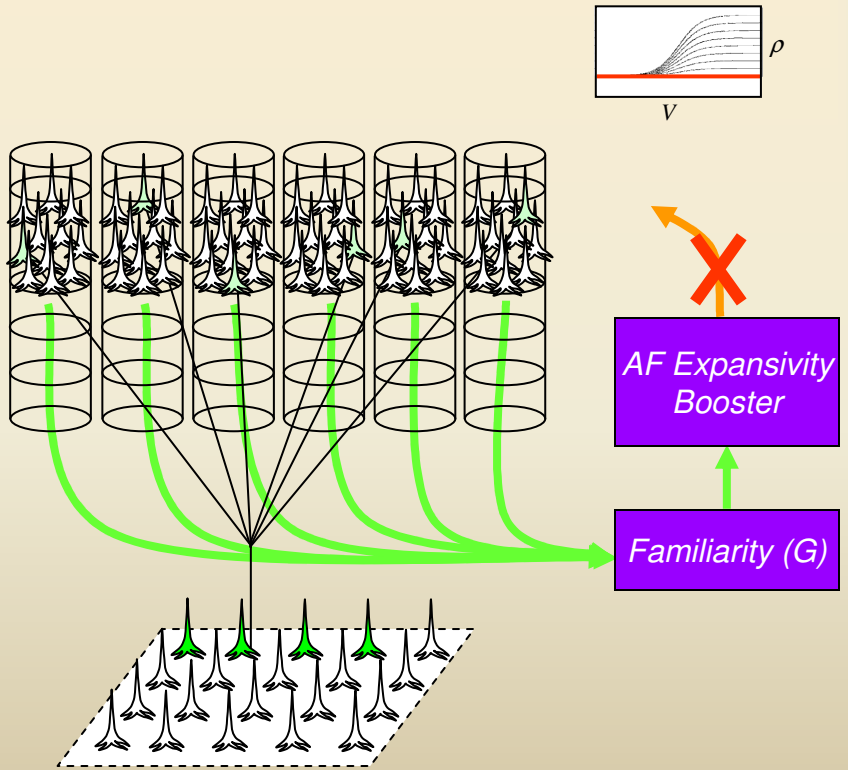
The expansivity of the sigmoid activation function (AF) must be set very high so as to strongly favor cells with high total normalized input summations (V) to win in their respective minicolumns.



Highly novel (G ≈ 0)

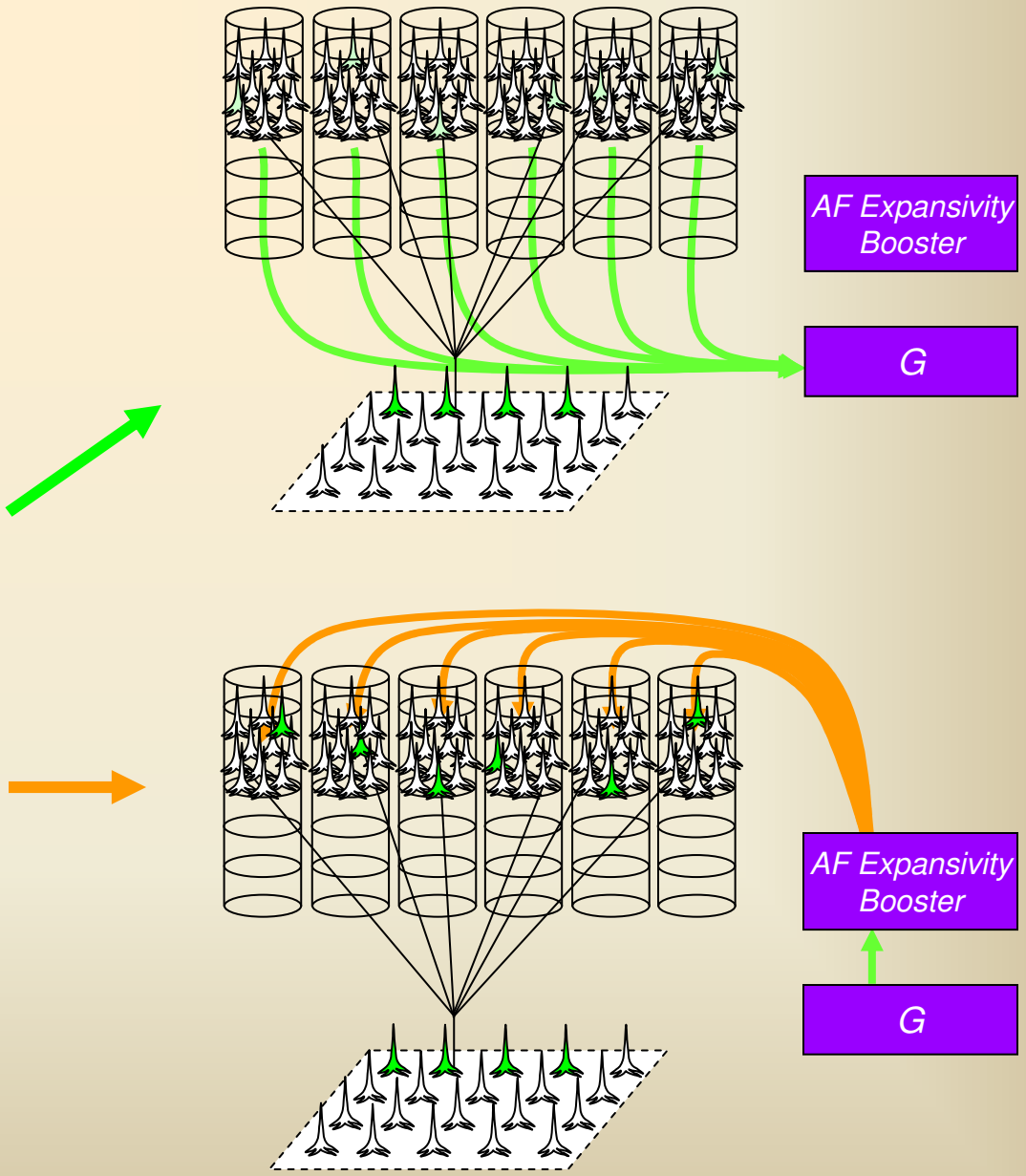
Should choose winners nearly uniformly randomly.

If we assume that the baseline AF of cells is a very compressive nonlinearity, and in the extreme, even a constant (flat) function, then no signal actually needs to be sent back to the minicolumns. There baseline operational mode will result in a random set of winners.



Implication

- Principal cells undergo ***two*** rounds of integration and competition within the basic computational cycle.
- The first round results in the activation of a ***preliminary*** code which drives the computation of G
- The second round is carried out after the AF expansivity is set as a function of familiarity, G, and results in the ***final*** code for the cycle.

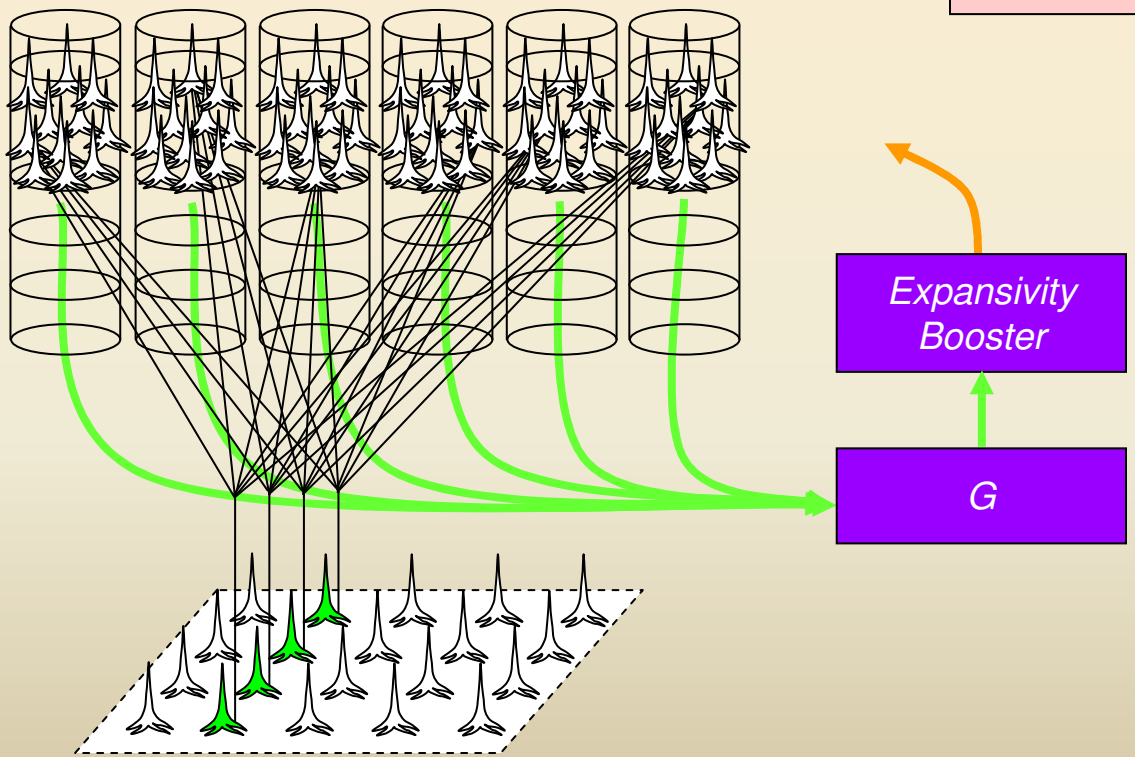


Modulating the Expansivity of the Activation Function Or, Modulating the amount of Noise (Randomness) in the Winner Selection Process

- Neuromodulators
  - Norepinephrine (NE)
  - Acetylcholine (Ach)
- Which one? Both? (cf. Briand et al. 2007)

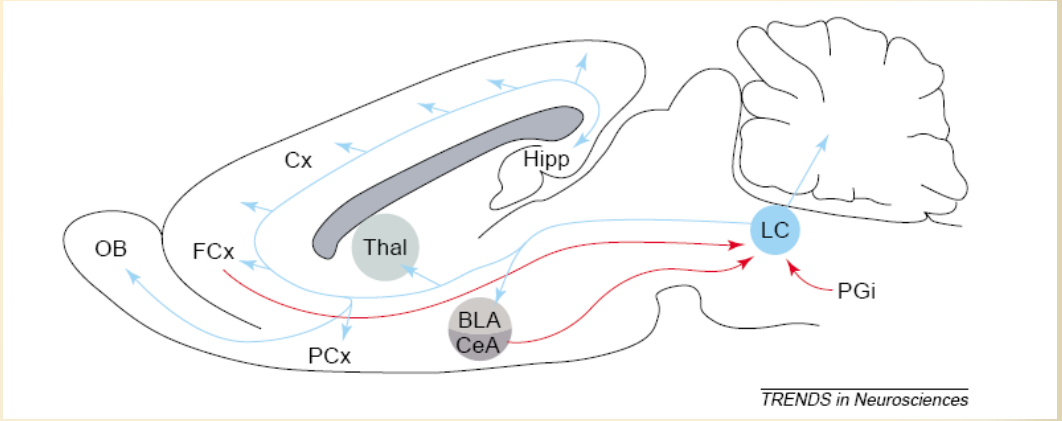
Related

- Levy & colleagues (1989 to pres.)
  - Randomization in choosing CA3 codes
  - …but not a function of familiarity
  - Controlling relative strengths of afferent vs. intrinsic inputs to CA3

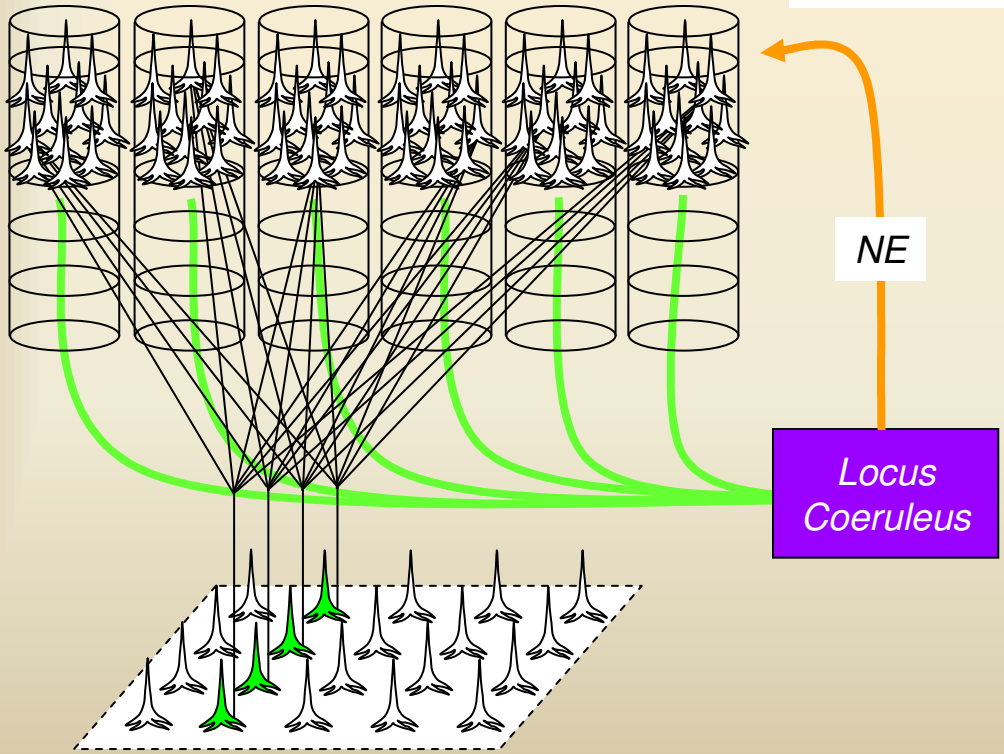


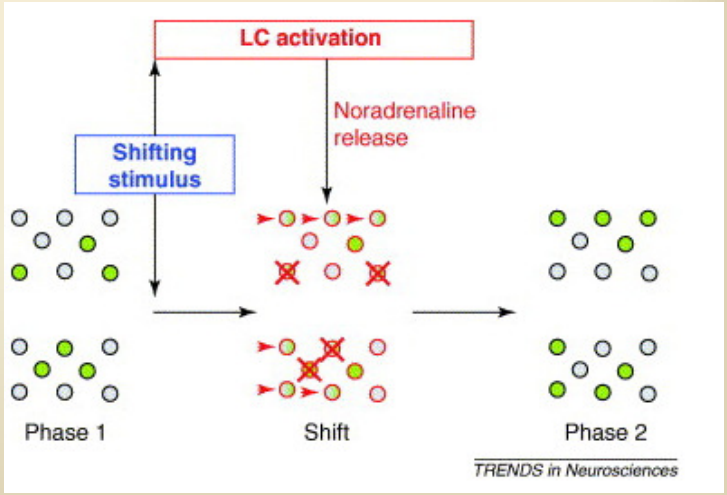
Suppressing LC Correlates with Increased Randomness in Winner Selection

- Low familiarity (high novelty)
- Low Phasic Norepinephrine (NE)
- High noise (randomness)
- Establishment of new neural codes



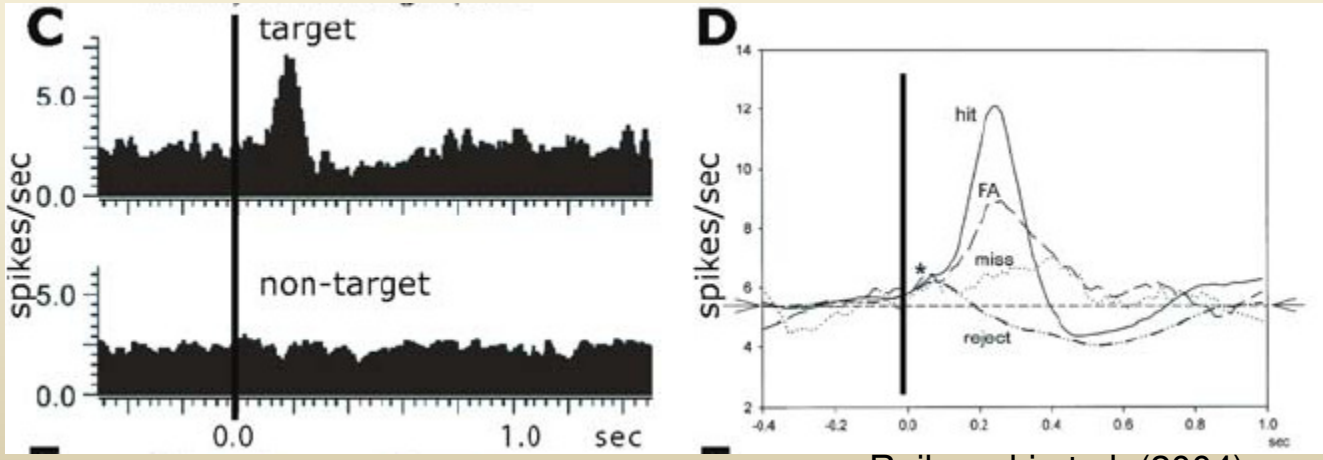
- Bouret & Sara (2005)





NE Data

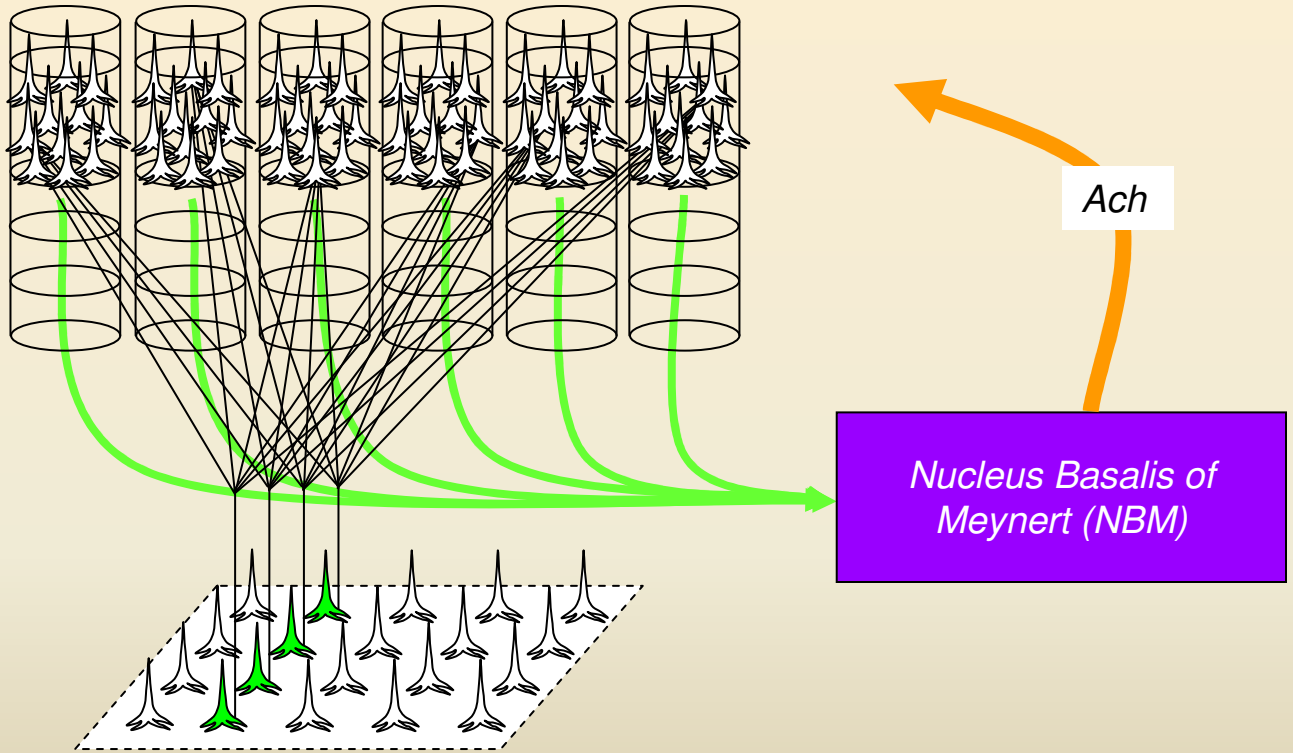
- LC activated by novelty: Vankov et al. (1995)
- Phasic NE: latency (~100-200 ms), short duration (~100-200 ms): Clayton et al. (2004)
  - Signals “unexpected uncertainty”, i.e., novelty. Dayan & Yu (2006)
  - Increase signal/noise (cf. Hasselmo et al. 1997)
  - “provoke or facilitate dynamic reorganization of target neural networks, permitting rapid behavioral adaptation to changing environmental imperatives” - Bouret & Sara (2005)
  - NE burst causes rapid state shift in hippocampal network: Brown et al (2005)
- PFC sends fibers back down to LC (Arnsten & Goldman-Rakic, 1984; Sara & Herve-Minvielle, 1995; Jodoj et al., 1998).



-Rajkowski et al. (2004)

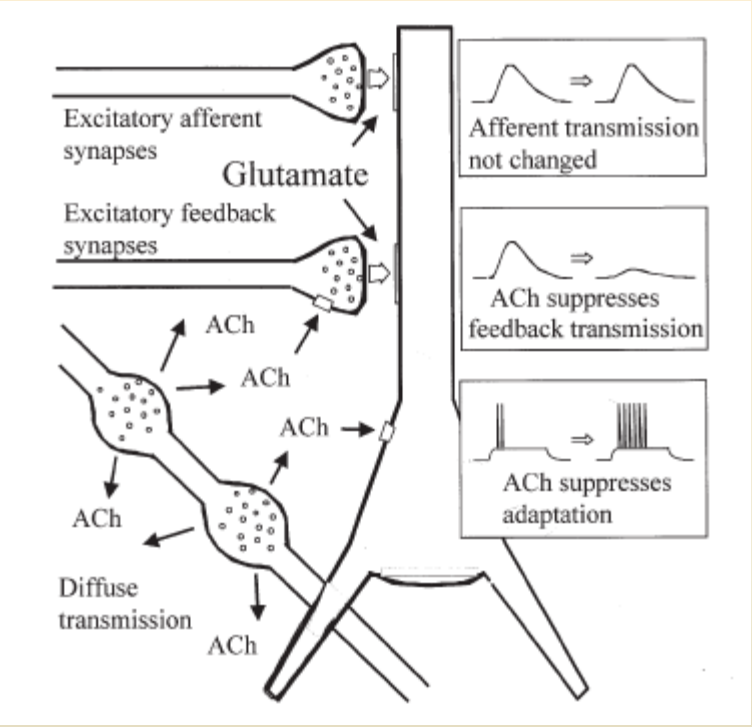
Increasing Randomness of Winner Selection: Ach

- Low familiarity (high novelty)
- High acetylcholine (Ach)
- High noise (randomness)
- Formation of new codes

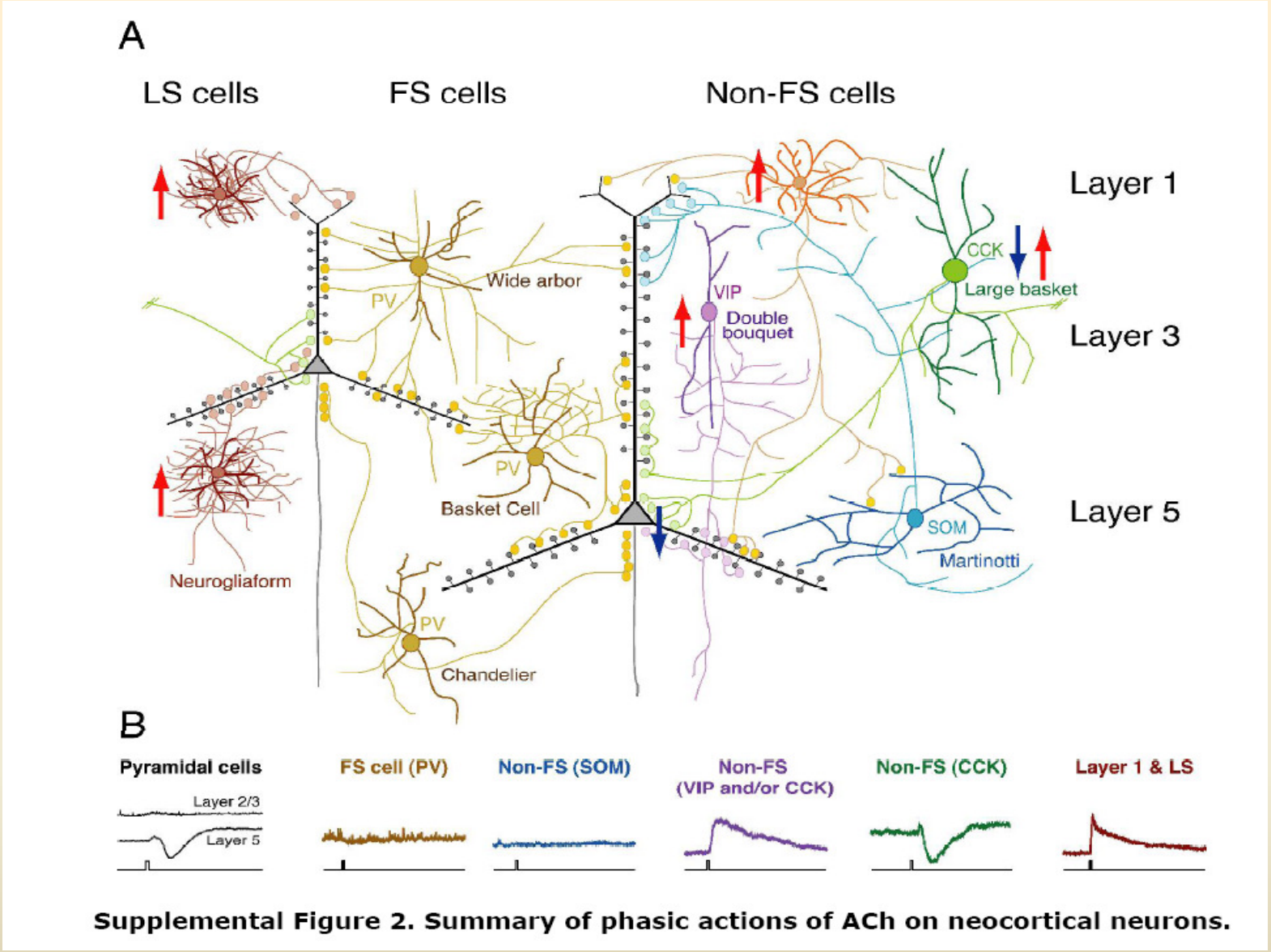


Ach Data

- Acetylcholine, not NE, is the main regulator of the level of spontaneous activity of cortical neurons: Isakova & Mednikova (2007)
- Kimura, Fukada, Tsumoto (1999): Ach causes:
  - synaptic facilitation,
  - synaptic suppression,
  - direct hyperpolarization,
  - direct depolarization
- ACh increases depolarization, excitability, and reduces spike frequency adaptation:
  - Tateno et al. (2005)
  - Hasselmo
- Increased Ach leads to learning of finer categories (more detail)
  - Olfactory - Linster et al. (2001)
  - Auditory – Weinberger et al. (2006)



- Hasselmo & McGaughy (2004)



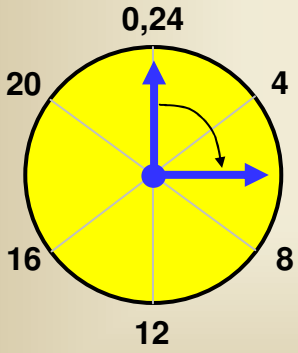
Supplemental Figure 2. Summary of phasic actions of ACh on neocortical neurons.

From Gulledge et al 2006 (Heterogeneity of ….)

Rough sketch of Possible Circuit

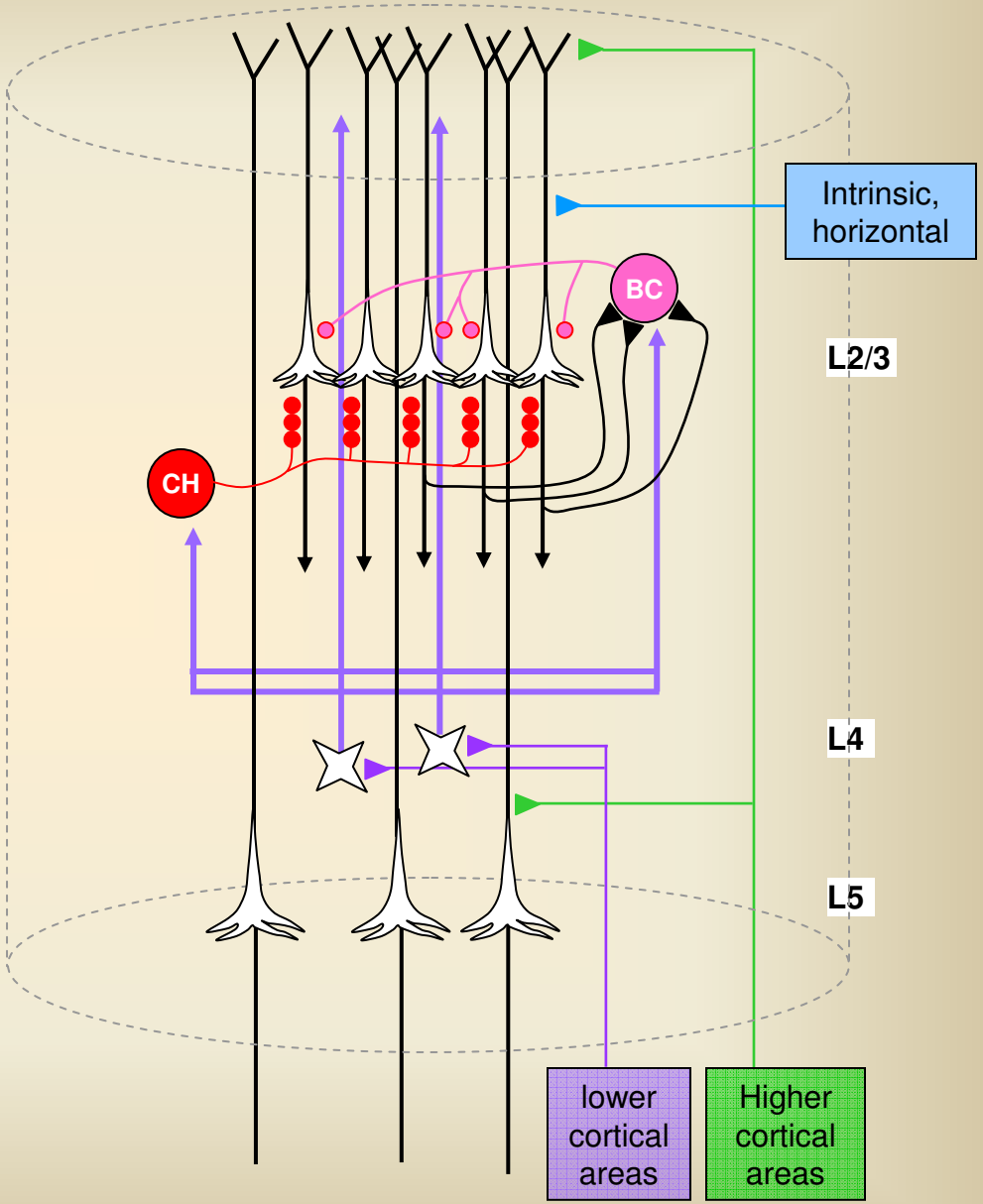
- L2/3 pyramidals integrate inputs
- Baskets integrate
  - BU inputs from L4 stellates
  - recurrent inputs from L2/3 cells.

- Chandeliers fire 1-3 ms after other FS interneurons (e.g., baskets) - Zhu et al. (2004)
- Chandeliers (in hippocampus) fire preferentially after strong, synchronized pyramidal activity (at Θ scale) - Klausberger et al. (2003)
- Chandeliers target only pyramidals – Peters (1984)



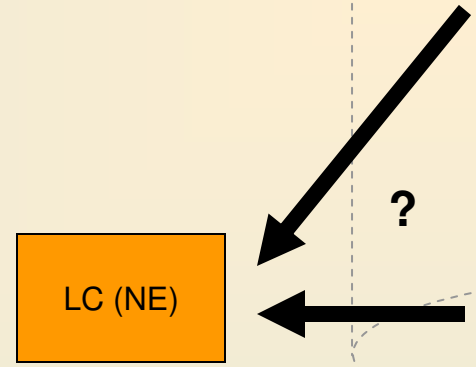
Gamma (ms)

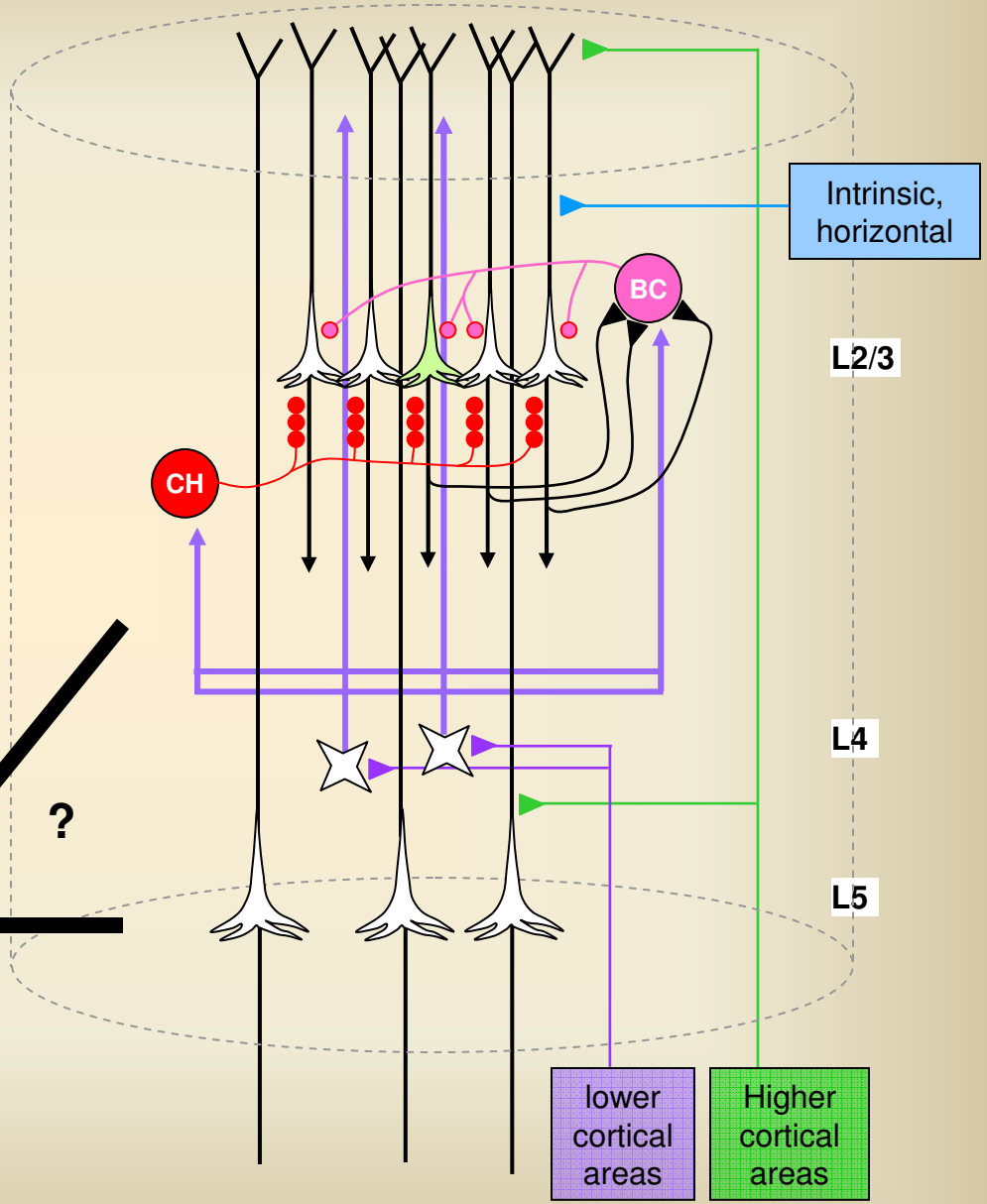
LC (NE)



Rough sketch of Possible Circuit

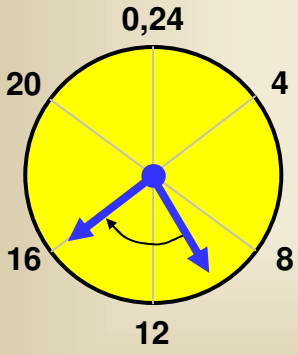
- *Preliminary* L2/3 winner emerges
- Interneurons squash other L2/3 pyramidals.
- Winner's output to LC (and maybe NBM)
  - perhaps via L5/L6
- How is winner's strength of activation communicated?
  - Spike frequency?
  - First spike latency?





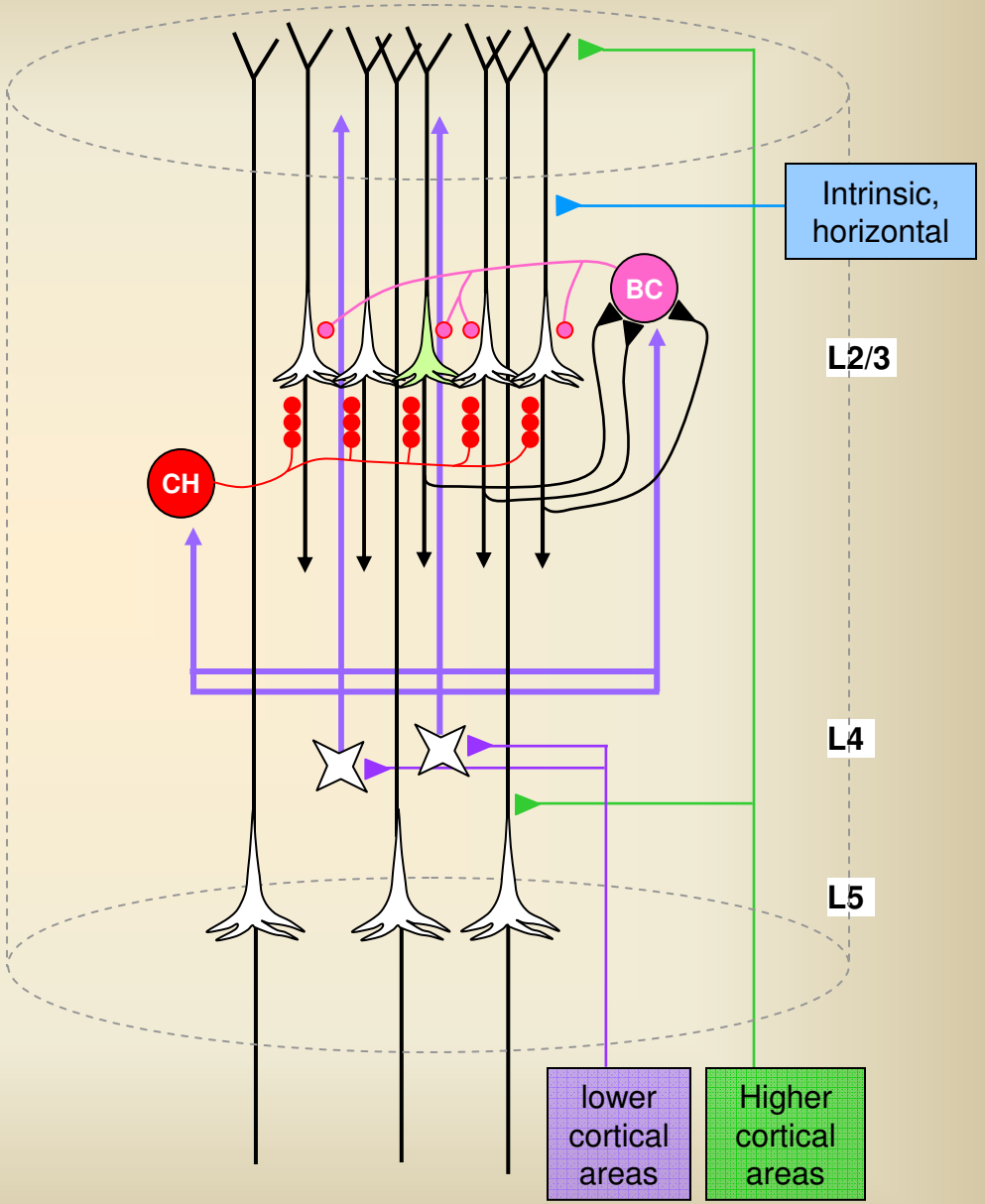
Rough sketch of Possible Circuit

- Average strength of activation of winners over whole macrocolumn, G, computed.
- Where is G computed?
  - LC
  - Perhaps NBM also?
- LC cells integrate and fire releasing NE back in cortex



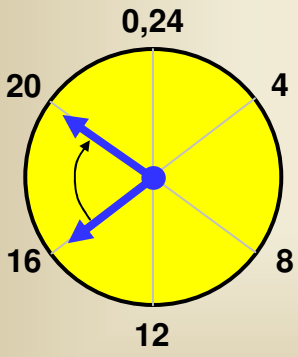
Gamma (ms)

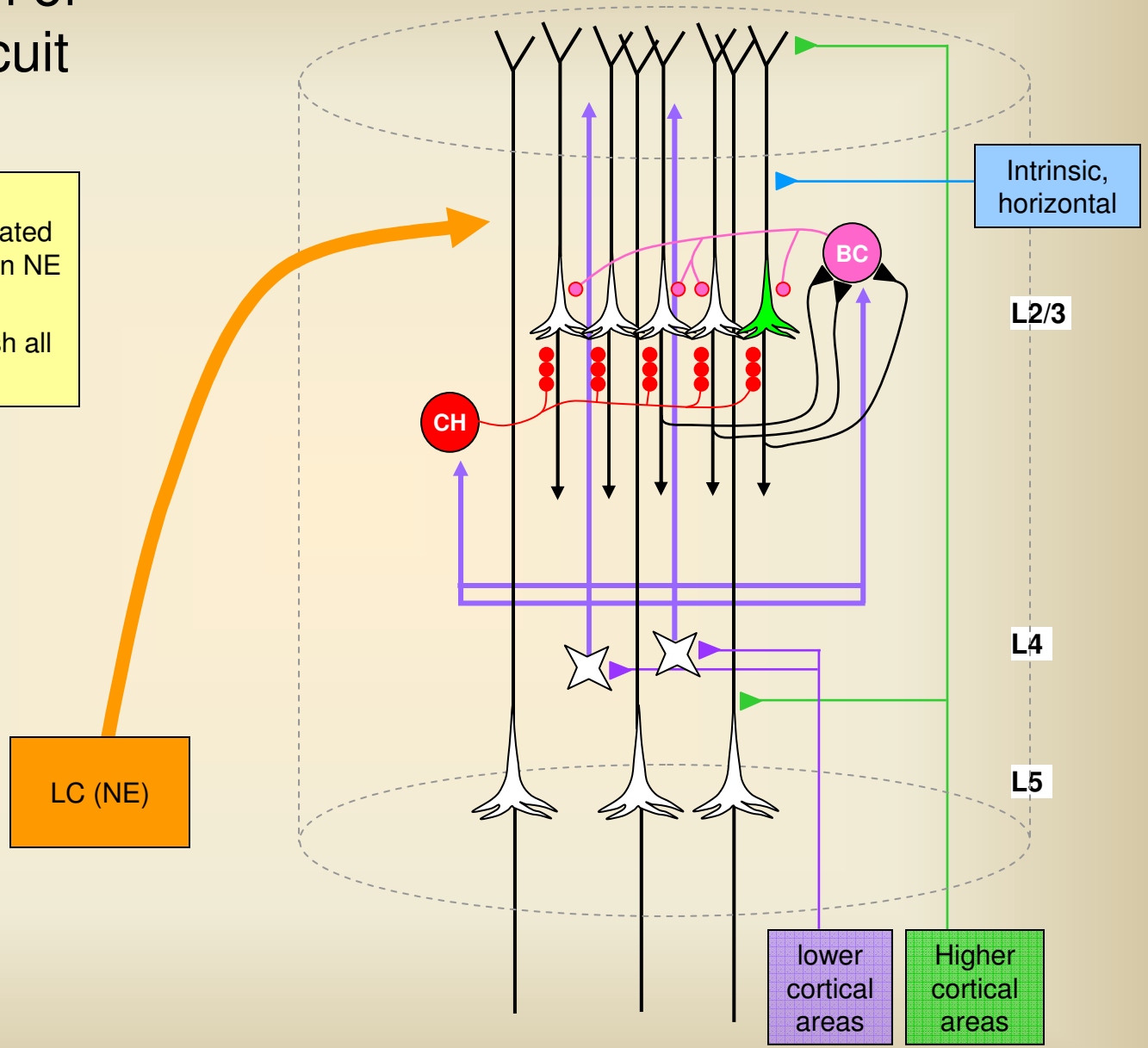
LC (NE)



Rough sketch of Possible Circuit

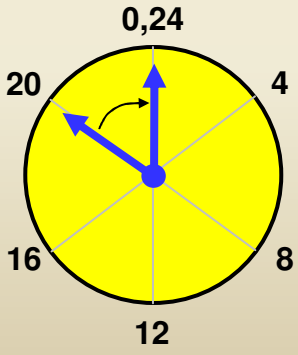
- Final round of integration and competition in L2/3, with modulated activation function depending on NE (and possibly) Ach levels.
- Interneurons engaged to squash all but one L2/3 pyramidal cell.





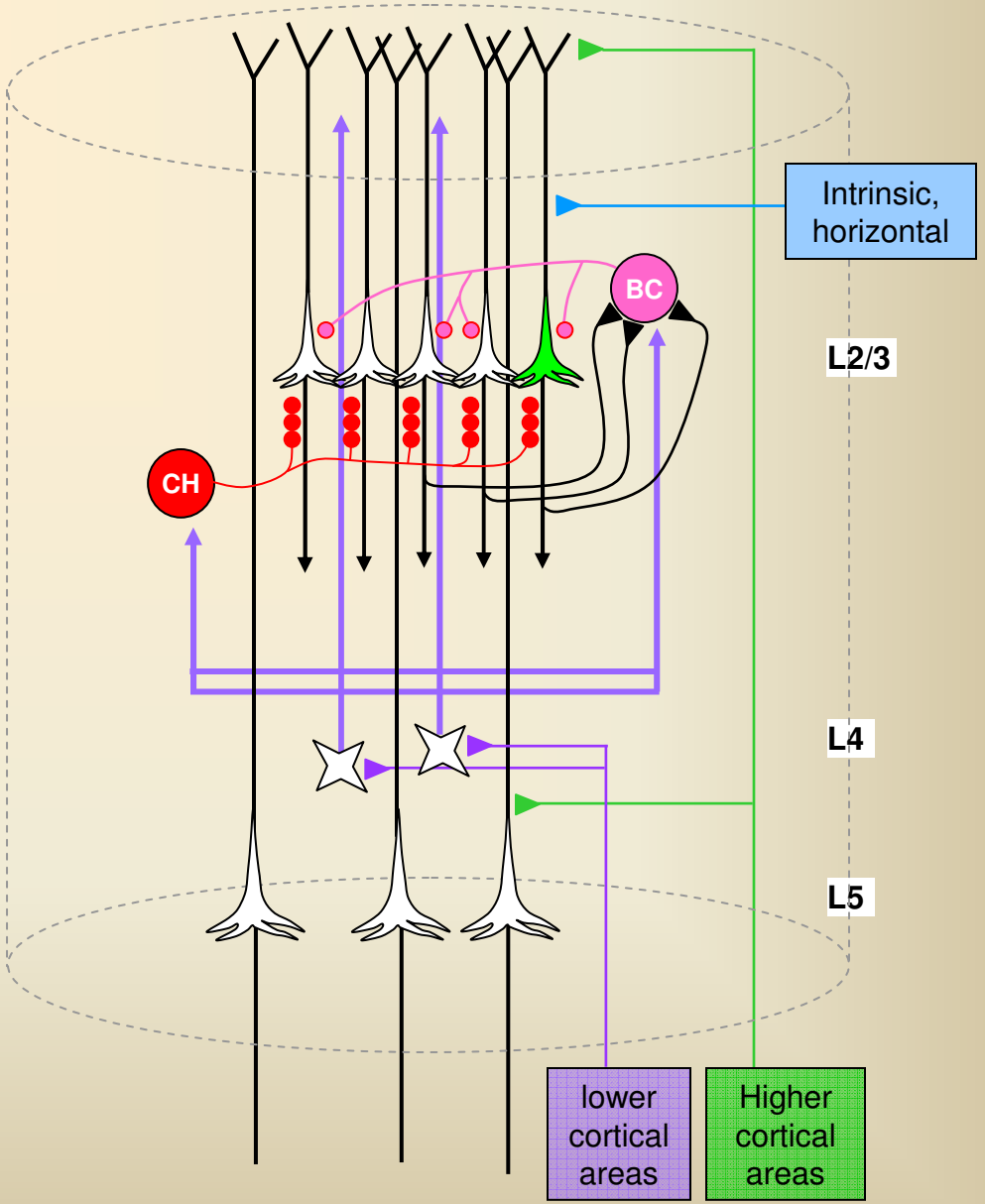
Rough sketch of Possible Circuit

- Final winner fires strongly, sending output to higher cortical areas (BU), lower cortical areas (TD) and horizontally (H) locally in the same cortical area.
- Activity-dependent learning to/from the final winner occurs.



Gamma (ms)

LC (NE)



Issues

1. NE, release latency is ~100-100 ms from detection of match between expected and actual input.
    - Theory requires sub-gamma time scale, i.e., ~10 ms, latency.
    - Solution: NE release depends only on results of algorithm running in PFC, ***NOT*** earlier cortices.
    - Similar consideration for Ach.
- No direct data that minicolumn functions as a WTA module
    - Experimental methods cannot resolve the question yet.

Questions

1. Do the baskets implement WTA in L2/L3?
2. Do the chandeliers keep L2/L3 pyramidals from firing while winners are being determined, i.e., during integration of inputs?
3. Are the chandeliers used to prevent firing during both rounds of integration?
4. Do large and small baskets have distinct functional roles?
5. Must the round 1 (prelim.) winners be completely inhibited (i.e., back to some baseline) prior to the second round of integration, or not?
6. Rather than supposing that the same minicolumn sub-population, the L2/3 pyramidals, is engaged twice in quick succession during a single cycle, could it be that the first round occurs in L2/3 and the second in L5 (or L5/6) (see next slide)?
7. Which cortical cells send axons to LC and NBM (or BFCS)?
8. Assuming that L2/3 is used for both rounds of representation in a cycle, preliminary and final, why would no learning occur onto cells that win in the first round?

Douglas & Martin (2004) Neuronal Circuits of the Neocortex"

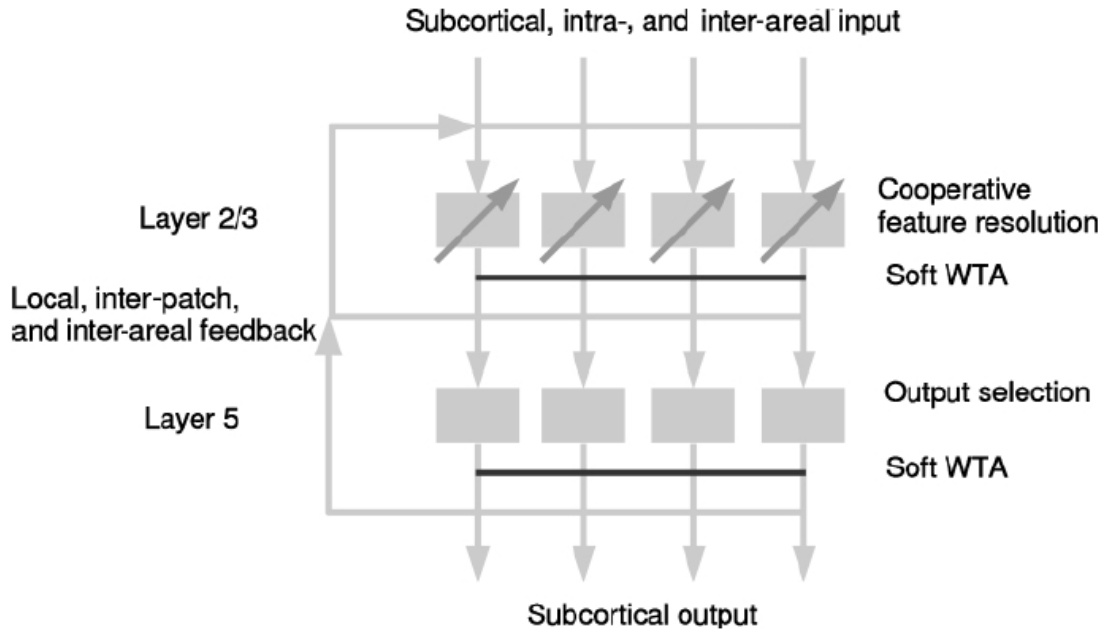


Figure 6 Simple model of cortical processing incorporating the principal features of cortical circuits. A patch of superficial pyramidal neurons receive feedforward input from subcortical, inter-areal, and intra-areal excitatory sources. They also receive recurrent input from other local superficial and deep pyramidal cells. These inputs are processed by dendrites of the superficial pyramidal neurons (*upper gray rectangles*, layer 2/3) whose signal transfer properties are adjusted dynamically by the pattern of vertical smooth cell inputs (*oblique dark gray arrows*). The outputs of the superficial pyramids participate in a selection network (e.g., soft winner-take-all mechanism) mediated by the horizontal smooth cells (*upper horizontal dark gray line*). These outputs of the superficial pyramids adjust the pattern of vertical smooth cell activation. In this way, the superficial layer neurons within and between patches, and within and between areas, cooperate to resolve a consistent interpretation. The layer 5 pyramids (*lower gray rectangles*) have a similar soft selection configuration (*lower dark gray line*) to process local superficial signals and decide on the output to motor structures.

What's Important

- The model
  - Efficiently assigns sparse distributed codes to inputs with single-trial learning
  - Efficiently retrieves the closest-matching stored code given an input
  - Plausibly maps onto minicolumn/macrocolumn anatomy and physiology
    - Plausible function of the cortical microcircuitry
    - Plausible usage of the neuromodulators, especially NE and Ach.

What's Essential

- The overall algorithm
  - Sparse distributed codes
  - Computation of a global measure of familiarity (G).
  - Increase of activation function expansivity in direct proportion to G.

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